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Emerging technology as new-life style. 3D Bioprinting, a new era for innovation process.

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Dissertation

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Abstract

3D Printing, an old concept, is today more important than ever. This technology offers transformative advantages at every phase of creation, especially within the emergence of the term 3D Bioprinting. This work focuses attention exactly on the additive manufacturing of human's organs, reflecting high potential paradigms behind of this specific technology in the Portuguese overview of the subject.

The premise of three dimensional Bioprinting comes from the possibility, to create exclusively with the purpose of design functional human organs, by allying three-dimensional Bioprinting technology with stim cells. The goal is definitely to build living human tissues that can function exactly like the native tissues each human has.

It opens a large amount of assumptions, constrains, problems but at the same time solutions come along, this advanced technology is always one step ahead day after day. The main purpose of this dissertation is to analyze the many variables associated with this technology, considering the context and perceptions of the Portuguese Medical Universities.

Trying to separate fictional from reality of 3D Bioprinting is very hard, to establish ambitious goals but yet realistically goals is extremely tough when discussing a subject such this one.

Many of the results from this dissertation can be seen as simple predictions of the future. However, 3D Bioprinting can be defined as disruptive type of Innovation, so it is only fair to mention the possibility to be a breakthrough in the Medical procedures.

Keywords: 3D Bioprinting, Organs, Innovation, Portugal, Medicine students

JEL-Codes: I19, Z19

Resumo

Impressão 3D um conceito antigo, é hoje mais importante do que nunca. Esta tecnologia oferece vantagens transformadoras em todas as fases da criação, especialmente a quando o surgimento do termo "3D Bioprinting". Este trabalho focaliza a atenção exatamente sobre a fabricação aditiva de órgãos humanos, refletindo os elevados paradigmas potenciais por de trás desta tecnologia específica no panorama Português.

Com a premissa do "bioprinting tri-dimensional" aparece a possibilidade exclusiva de concretizar o ambicioso propósito de criação de orgãos humanos funcionais, conciliando células estaminais com a tecnologia "3D Bioprinting", cujo objetivo final será a construção de tecidos humanos vivos, que poderão funcionar precisamente como os tecidos nativos que cada ser humano possui.

"3D Bioprinting" partilha enorme quantidade de suposições, constrangimentos, problemas, mas ao mesmo tempo cria-se novas soluções para problemas existentes, esta tecnologia avançada está sempre um passo à frente a cada dia que passa. O objetivo principal desta dissertação é analisar as muitas variáveis associadas com esta tecnologia tendo em conta o contexto e perceção dada pelas Universidades de Medicina Portuguesas.

É muito difícil separar ficção da realidade na questão do "3D Bioprinting", principalmente se estabelecemos metas ambiciosas, mas ainda de forma realista tornando-se extremamente complexo quando se discute um assunto como este.

Muitos dos resultados desta dissertação podem ser vistas como simples previsões do futuro, "3D Bioprinting" pode ser definido como um tipo de rutura de Inovação, e por consequência é adequado mencionar a possibilidade de ser um grande avanço nos procedimentos médicos.

Palavras-chave: 3D Bioprinting; Orgãos humanos; Inovação; Portugal; Estudantes de Medicina.

Acknowledgments

"There is no passion to be found playing small" (Nelson Mandela)

I want to take this opportunity to express my gratitude to some special people that supported my decisions and even when I made a lot of mistakes, always keeping forward without feeling any regrets from the past, learning from these mistakes to become a better person.

Firstly my parents, mama and papa you are the best parents I would wish for, this can be "cliché" but they are truly the most honest and fair people I know. Thank you for every single value that you taught me, and betting so much on my education, I hope to make you proud someday. No matter how badly I failed, always treat me like a winner. Thanks for being so supportive even under sickness and sadness moments!

My friends, the family we choose, thank you for being there on the most crucial moments, in special my 2 best friends; Diogo and Pedro, we know each other since little boys sometimes we have our very extraordinary discussions, and I must say, if I could I would wish to have 2 brothers like you both. Thank you for all the support my brothers for life!

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Index of Contents

Index of Tables

Index of Figures

Introduction

3D Printing is an innovative technology, allied to health field in which the term "Bioprinting" emerged, leading to a new type of mentality. Nowadays, there are many reasons to believe that in the near future this technology can show up as a revolutionary saving-life tool. The improving quality of life might change overnight and become the most important forthcoming goal (Mironov et al., 2008).

The purpose of this dissertation will be the study of the potentials of 3D bio-printing technology, highlighting the reproducing of 3D human's organs (Seedhouse, 2014), integrating scientific concepts lectured on the Master in Innovation and Technology Entrepreneurship at FEUP (Faculty of Engineering of University of Porto, Portugal). Furthermore, it aims to investigate the assumptions that can distinguish the frontier between reality and fiction (Guillemot, Mironov, Nakamura, 2010). In addition, there is an opportunity to demystify the idea that not always the artificial is malicious to the health and in this case it is quite the opposite it can actually save lives (Lipson et al., 2013).

Imagine, in short term, the possibility of having fast and efficient answer to a transplant, (Nakamura, 2010) avoiding long waiting lists and the dependence of compatible donors, since the organs are custom made to fulfil patients' needs; or perhaps a baby that had the misfortune to be born with some heart condition. "On 2011 the surgeon and regenerative medicine pioneer, Dr. Anthony Atala gave a talk at the Annual TED conference", where he demonstrated on stage a special 3D printer that was building a prototype human kidney. He explained that the increasing health crisis that is arising as people live longer and organ failure becomes more common. In fact, one of the biggest problems that mankind have these present days, is to really find a compatible organs transplant for the growing number of patients and diseases (Barnatt, 2013).

3D Bioprinting could be the answer to solve many problems, with endless opportunities. This technology can express much more than a simple life change, it represents a disruptive or radical type of innovation (Dewar, and Dutton, 1986) which includes the studying of a new market, new assumptions, and new knowledge in different sectors.

This opportunity emerges to contextualize the Portuguese market, allowing a new biomaterial paradigm, enabling to understand if it is possible the development of a market plan highlighting advantages and disadvantages as well feasibility concerns.

This study contributes mainly at empirical scientific level, not excluding the possibility of any forthcoming gaps in Portuguese dimension for this specific sector. Firstly it will use several databases in which are included scientific studies, articles and books that were already been published to do a literature review. Then, it focuses on additive manufacturing (AM) of human organs. AM is defined as the "process of joining materials to make objects from 3d model data, layer upon layer, as opposed to subtractive manufacturing methodologies, such as traditional machining"- (Atala, 2009). Beyond this it is quite obvious the need to create a survey as one of the most important methodology, to share several points of views inside of the medical community, keeping in mind the Portuguese dimension in terms of market for this kind of technology inputs.

Nowadays much of this technology is still in laboratory, but as far as one can see, gradually many real-cases have been reported that may easily explain how important is to look forward. If today it is possible to save a baby with a simple 3D modelling procedure, what can be achievable in 10 or 20 years?

1. Literature review

1.1. Innovation

Innovation has been frequently used to express the application of better solution that encounters new requirements, and it can be accomplished through product, processes, services, technology or ideas. “The notion that innovation begins with a discovery in “basic science” proceeds with an application or invention derived from this fundamental work (“applied science”) and ends with the development of a new product or process (an “innovation”) was indeed at one time quite influential.” (Freeman, 1996).

Furthermore “innovation is the specific tool of entrepreneurs, the means by which they exploit change as an opportunity for a different business or service. It is capable of being presented as a discipline, capable of being learned, capable of being practiced”. (Drucker, 1985). The implementation of a technology by itself often requires solving complex problems. Schumpeterian literature usually refers that “entrepreneurs will seek to use technological innovation – a new product/service or a new process for making it – to get strategic advantage. Joseph Schumpeter called it “monopoly profits”, and usually refers that innovation is a process not an event which means there is an opportunity to see what has been done and try to imitate it – with the result that other innovation emerges. Schumpeter “talks of a process of ‘creative destruction’ where there is a constant search to create something new which simultaneously destroys the old rules and established new ones – all driven by the search for new sources of profits” (Schumpeter, 1950).

Innovation is an important concept to understand and it contributes in different aspects: for example, evidence suggests a strong correlation between market performance and new products (Souder and Sherman, 1994). Creating innovative products help to capture market shares, increasing the profitability in those markets. In case of mature and established products, competitive sales growth doesn’t necessary depend only on the price but also on non-price factors – design, customization and quality. “Competing in time reflects a growing pressure on firms not just to introduce new products but to do faster than competitors” (Rosenau et al., 1996) – “Companies achieve competitive advantage through acts of innovation. They approach innovation in its broadest sense, including both new technologies & new ways of doings things” (Porter, 1990)

Nowadays in terms of technological innovation, appeared a definition called “open hardware”. Open source hardware “is about open sourcing innovation, and also democratizing innovation, but does not come with 20 years of exclusive rights (Anderson et al., 2006). The benefit is that you have an entire community contributing to your designs, innovating, and sharing their derivatives to your product. It pushes the original designer to create a better product and continue to improve it rather than lock it in a 20 year stalemate.”(Pearce, 2012). Open source “philosophy” works perfectly for relatively complex products, such as software and electronics. Only few people can improve someone else’s complex circuit or algorithm, so the original designer usually still stays in control of the project even after it is released. As an example of this open source “philosophy” and according to Bioprinting subject it is already possible to download a portable document file (pdf) denominated “instructable” that teaches how to convert a standard inkjet printer into a device that can print out cells.

“Many great technological innovations that are created for one purpose end up being used for another.” (Barnatt et al., 2013) It may be the case of ‘product innovation’, that is, changes in the things (products/services) which an organization offers; in addition, there may be a ‘process innovation’, meaning there are changes in the ways in which products are created and delivered. We can also consider ‘position innovation’, which represents changes in the context in which the products/services are introduced; finally, the ‘paradigm innovation’ refers to changes in the underlying mental models which frame what the organization does”.(Tidd and Bessant, 2013)

1.2. Emerging Technology

Why some technologies shake up the world while others doesn't affect our daily live often? (Anderson, 2008) Burst of innovation take place when an emerging technology removes a once prohibitive barrier of cost, distance or time. In the case of (e.g.) 3D printing, it shrinks two prohibitive costs to zero: the cost of customization and the cost of complicated shapes.

Emerging technology is distinguished from the conventional technology; (Scheufele and Lewenstein, 2005), "acquiring preemptive knowledge about emerging technologies is the best way to ensure that we have a say in the making of our future" (Mota, 2012); Emerging technologies can be defined by highly capability of technical innovation which represents progressive developments within a field for competitive advantage. (Lewenstein et al., 2005)

Technology can help target and qualify the emerging markets and it is often related to create the perfect conditions, tools and concepts while this term "emerging technologies" is still used without a clear meaning or definition.

Emerging technologies are evolving organisms that experience hype cycles, while at the same time being potentially disruptive, not yet fully understood, and not yet fully researched. (Veletsianos, 2010). The impact of technological innovation and advancements have brought massive social change (Gazit and Cooper, 2011). "What is discontinuous about the moment of radical technological change? Discontinuity typically does not lie in a radical advancement in technology itself; rather, the discontinuity stems from a shift of an existing technical lineage to a new domain of application. Seeming revolutions such as wireless communication and the internet did not stem from an isolated technical breakthrough". (Adner and Levinthal, 2002). "The implementation of new technologies, products, or business models that represent a dramatic departure from the current state of the art in the industry" (Bessant et al., 2006).

Emerging technologies are contemporary advances such as the example of Innovation; it can also be characterized as a process not a invent – "One of the problems in managing innovation is variation in what people understand by the term, often confusing it with invention. In its broadest sense the term comes from the Latin – innovare – meaning 'to make something new'. Innovation is a process of turning opportunity into new ideas and

of putting these into widely used practice" (Wilson and Stokes 2010). Emerging technology needs innovation to survive. (Porter, 1990).

"Emerging markets and emerging technologies present challenges and opportunities for businesses and individual entrepreneurs who focus their firms for competitive advantage on them" (Tidd and Bessant, 2012).

3D Bioprinting definitely may be seen as an emerging technology for constructing and fabricating artificial tissue and organ constructs. "This technology surpasses the traditional scaffold fabrication approach in tissue engineering (TE).

Currently, there is a lot of research / investigation (e.g. Atala, 2011) being done on Bioprinting technology and its potential as a future source for implants and full organ transplantation. (Forgacs et al., 2012). Once more this emerging technology appears to be more promising for advancing tissue engineering, toward functional tissue and organ fabrication for transplantation, looking forward in order to save lives. (Ozbolat and Yu, 2013)

1.3. Time to Market

What does "time to market" mean? Usually it defines the period of time it takes from a product being conceived until it is being available for sale (Kenneth, 2004). Timing of market entry is a critical decision, involving the need to make a distinct premeditation and balance the risk of premature entry with the problems of missed opportunities as a result of late entry (Lilien and Yoon, 1990; Castro and Chrisman, 1995).

"Predicting future markets for the 3D technology printed goods and services is an equally daunting task. It is difficult – almost impossible – to offer a few crisp words that sum up potential new business models that offer good, fast and cheap products or services to their customers" (Lipson and Kurman, 2013).

A few decades, it may become possible to use a Bioprinter to drastically, quickly and fairly safely transform the human body (Atala; 2012; Bernatt 2013). Many questions can be answered: (e.g. Dr. Atala conference, 2011). "Want bigger muscles without exercise? Then why not visit your local Bioprinting clinic and have them printed into your body that afternoon? Or fancy going skiing but worried about breaking your legs? Then why

not have your bones replaced with new one that features carbon nanotube enforcements? These top-of-head scenarios may sound both fantastical and scary. Yet they may well be just the tip of a cosmetic Bioprinting iceberg". (Barnatt et al., 2013)

The fact that Bioprinting is now both a hobbyist and professional pursuit does strongly suggest that more concepts can emerge (Barnatt, 2013).

In 2014 there are currently "123.175 people waiting for lifesaving organ transplant only in United States of America (U.S.). Of these, 101.170 await kidney transplants, on average nearly 3,000 new patient are added to the kidney waiting list each month. 12 people die each day while waiting for a life-saving kidney transplant, every 14 minutes someone is added to the kidney transplant list. In 2013, 4.453 patients died while waiting for a kidney transplant" (National Kidnay foundation, 2014). In Portugal by the end of 2014, there were 1970 patients waiting for surgery, the number of new patients on the waiting list for kidney nearly double last year. "Portugal, along with Turkey, is the country that has the highest rate of new patients." (Newsletter Transplant, 2015)

The newsletter of the Council of Europe places Portugal in the fourth place in the organ searching and in the 10^{th} place in transplantation. In 2015, 81 patients died while waiting for the transplants, 43 died waiting for a compatible kidney. "The kidney transplantation face several problems, beside the increase of patients, there is less use of harvested organs." (Portuguese Institute of Blood and Transplant, 2015)

The fast appearance of commercially Bioprinters can be definitely considered one of the most remarkable developments of the past decade. The exponential progression of different deviations of Bioprinting technology resembles the early development phase of "AM (Additive Manufacturing) technology two decades ago, when many competing technologies were developed but not all of them were successfully commercialized (Atala et al., 2012). Robotic Bioprinters are already commercially available, while others are still under development. The 3D Bioprinters currently on the market can cost around $100–200 thousands, depending on their unique capabilities, while 3D homemade Bioprinters can cost less than $20 thousands" (Ozbolat and Dababneh, 2014).

As some authors referenced, the success behind emerging technologies comes from "looking at existing emerging technologies and pay particular attention to market niches that will accept the technologies in their present form".(Adner, 2002) -"Deploying

emerging technologies in these early markets can be a means of both realizing profits in the near term and providing valuable feedback regarding the demand for possible attributes of technical functionality to support and guide their further development."- (Adner, Levinthal, 2002)

Entrepreneurs have an important duty related with the introduction of new technologies in the market. (Gruber and MacMillian, 2007). "Technologies are often configurable to serve a variety of different markets, it is possible for entrepreneurs to identify multiple market opportunities *prior* to the first market entry of their emerging firms, and if they elect to do so, they therefore have a choice of which market to enter first". (Thompson, et al., 2007)

1.4. The Beginning of 3D Biopriting as creative disruptive technology

"3D Bioprinting has emerged to change the world" (Seol, Kang, Lee, 2014). It has many times been referred from several authors, as powerful tool for building tissues and organ structures (Atala et al., 2011) in the field of Biotechnology Engineering. Gabor Forgacs was one of the pioneers of this technology in 1996. Following a study of chicken embryos, he noticed that cells stick together during the embryonic development in a manner which makes perfect sense to assist in artificial tissue fabrication (Barnatt, 2013).

Alongside Gabor Forgacs, there is several others highly significant Bioprinting pioneers such as Makoto Nakamura -following the increasing number of patients desperate for an organ transplant (Ozbolat, 2013), Nakamura started to conjecture hypothetical way to offering hope for bridging the gap between organ shortage and transplantation needs. He begun by creating mechanical, inorganic prosthetics and "quite by chance he realized that the droplets of ink emitted from the print head in a standard inject photo printer are about the same size as human cells". So basically he just needed to turn a photo printer into a 3D Bioprinter using perhaps human cells as the "special ink" for the machine. In theory the process was complex but at the same time easy to understand. The printer could output the cells via a material jetting process that would eventually result in artificial, living tissue (Mironov, Boland, Tirusk, 2003). However, "the first experience in standard Epson photo printer" did not work as "the device's print head simply clogged up". It was necessary to modify the photo printer to successfully output cells that survived the inkjet

printing process. This was “achieved by encasing the cells in solidus alginate to stop them from dying out, and by jetting them into a calcium chloride solution”.

In addition to Nakamura and Forgacs, others researchers have managed to adapt standard inject printer mechanisms to demonstrate proof- of-concept Bioprinting. In this context, Thomas Boland and Vladimir Mironov were possibly some of the most notable researchers, having successfully conducted similar experiments.

The first commercial Bioprinting- NovoGen MMX- was developed by Gabor Forgacs, who founded in 2007 a company, called Organovo, with the mission to “create tissue on demand for research and surgical applications”. Two years later the MMX just needed sample of cells to be sourced from a patient biopsy or stem cells in order to have final volume of cells. Let us explain this technique more carefully: “ For example if a blood vessels is to be Bioprinted, an aggregate is created containing a mix of primary endothelial cells (which form the lining of blood vessels), smooth muscle cells (which allow blood vessels to expand and contract) and fibroblast (which form tough connective tissue) then the procedure is to compress like a kind of bio-ink “sausage” allowing an “aggregate cutter” to chop this sausage into bits, with the very tiny pieces spontaneously forming into bio-ink spheroids, each one containing between 10,000 and 30,000 individuals cells” (Gabor Forgacs et al., 2009). In December 2010, Organovo used NovoGen MMX to create the first Bioprinted human blood vessels while in the same year “Time Magazine” heralded the NovoGen MMX as one of the best inventions. Three years later it even reported the successful of Bioprinting human liver tissue. Organovo is considered one of the world´s 50 most innovative companies. It is already a publicly traded company, one of the only five 3D printer manufacturers of any genre to have this status.

Furthermore aggressive procedures such as replacement of entire soft-tissue organs, like kidneys or livers, can be possible, once Bioprinted patches and grafts enter clinical practice (Atala and Forgacs, 2012). The prediction for that to happen, as Dr. Atala and Professor Forgacs referred, it can be possible in 2018.

Many authors referenced the solution of turning a common 3D photo printer to Bioprinting, happened by quit chance,(e.g Nakamura and Forgacs, 1996) after all it turns to be one solution to probably solve several problems mainly related with organs transplant.(Atala et al., 2011). However one of the biggest barriers for that to happen is

the slow development of new drugs by the pharmaceutical companies, worldwide trials of next generation medicines are increasingly failing, labs frequently not living up to expectation, and also difficulty to find shareholders willing to give money for this kind of innovation.

A range of Bioprinting and related hardware has been developed, based at the Advanced Tissue Biofabrication Center at the Medical University of South Carolina, US. Mironov believes that any future Bioprinted heart will need significant workout in the lab by an appropriate machine before it is strong enough to pump blood around a human body just like the muscles, they become stronger as a result of exercise.

It is important that the technology is available in such a way that everyone can access to it when needed. In fact, some authors believe Bioprinting organs for human transplant shall be easy to be fabricated "at the click of a button" (Ozbolat Nakamura et al. 2012) which means that there should be an integrated friendly user interface software.

"Systems must be developed to transport nutrients, growth factors and oxygen to cells while extracting waste so that the cells can grow and fuse together, forming the organ. Cells in a large 3D organ structure cannot maintain their metabolic functions without this ability, which is traditionally provided by blood vessels" (Ozbola, 2012). The problem that must be overcome is the difficulty to Bioprint "microfluidic channels" that can take on the natural vascular network. Bioprinting a pancreatic organ that is glucose sensitive can be a good example (Forgacs, 2009) of how complex and hard is to perform this activity. It is expected in the medium-term to transplant such a Bioprinted organ into an animal to successfully "hook it up to its vascular system". In long-term the wish is to develop the "ultimate economical and feasibility technology" (Seol and Kang, 2014), allowing stem cells to be used, to Bioprinting a pancreatic organ that can be successfully transplanted to a human body, including the possibility of regulating the glucose level of the blood.

It is essential to make a distinction between additive manufacturing and rapid prototyping. (Petrick and Simpson, 2013). Both this terms refer to turn computer models into real solid objects by building with many thin layers (Barnet et al., 2013), but while rapid prototype is already been used for at least the last 30 years (creating concept of models or mold

masters), the application of this technology has been starting to widen to different sectors and so it appears the term additive manufacturing.

Many researchers worldwide share the belief that one day Bioprinting will result in a medical revolution allowing for the true meaning of disruptive technology. (Markwald and Forgacs, 2003; Bartolo and Jorge, 2007; Mironov and Boland, 2012)

Despite the enormous progress that assisted and many breakthroughs of the last decade, 3D Bioprinting technology is not mature enough, which means that it has met several challenges and limitations. Firstly, there is the problem of "repeatability, cell viability, practicality, and biocompatibility of Bioprinting processes cell density". There are also technical problems regarding the "cytotoxicity, bioprintability, solidificability and solidification speed, mechanical and chemical properties, affordability and abundancy, and cell viability and long-term cell functionality of bioinks compactness". In addition, there are issues related with "accuracy, high-degree-of-freedom motion capability and motion speed, commercial availability, full-automation capability, user-friendliness, sterilibility, affordability, and versatility of the bioprinters" (Dababneh and Ozbolat, 2014)

2. Methodology

This chapter presents and describes the methodological options, such as the research method and tools, the questionnaire design and formulation of the data collection process.

2.1. Identification of methodology and applied framework

It is relevant to understand how this technology can be applied to the daily life. To better understand this point it was required a test in the field. Based on the literature review, it was created a quantitative survey targeting all medical students in Portugal. The main goal here is to see how they react to the context and the meaning of this technology, considering the implications of it in the medical activity.

In order to achieve such an ambitious goal, it was needed the participation of 8 Medical University in Portugal, precisely 241 students participated in the survey and many others had the curiosity to try to understand what in fact 3DBioprinting is all about. The target of this survey was restricted only to the Medical Students in Portugal; however some of

the Erasmus Students (foreigners) did also answer the questionnaire but unfortunately the results from this were not meaningfully relevant to the case.

Quantitative methodology applied on this subject has been defined with the help from 2 main research questions:

- The first one related with the use of the 3DBioprinting in what terms and for what;
- The second related with the level of acceptance from the medical perception;

Several questions were asked in terms of the application of this technology and the most interesting results come from 2 main questions: if the "3D Bioprinting could be the answer for Transplants" or if the "3D Bioprinting could be the answer for new drugs investigation".

Table 1 groups the questions of the survey in 3 categories: awareness, application and expectation, each of whom will be discussed in the following section. The complete survey is presented in appendices 1 and 2.

Research question		The most relevant questions (Q) of the survey	Proposed analysis technique
3DBioprinting	Awareness	Q8,Q9,Q20	Frequencies, correlations and appropriated tests
	Application	Q10,Q11,Q12,Q14,Q17	
	Expectation	Q13,Q15,Q19	

Table 1 - Schematic of analysis statics

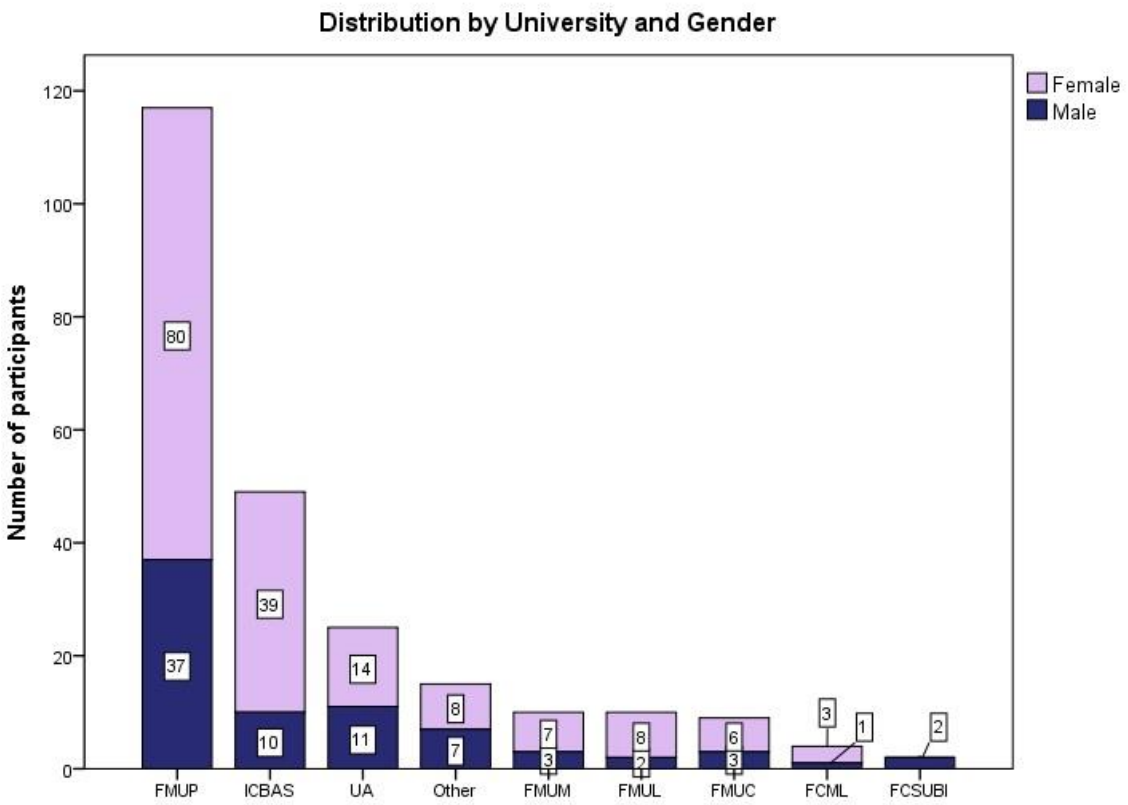

Figure 1 - Distribution by University and Gender

The ages of the participants are between 18 and 49 years, in which the average age is 24,21 and 4,33 is the standard deviation; 76 (31,5%) were male students and 165 (68,5%) female students, reaching the total of 241 surveyed. Figure 1 presents the number of answers by gender (female and male) in each university and the repartition of answers among Medical Portuguese Universities:

- FMUP (Faculty of Medicine of University of Porto)
- ICBAS (Institute of Biomedical Sciences Abel Salazar of U. Porto)
- UA (Algarve University)
- FMUM (Faculty of Medicine of University of Minho)
- FMUL (Faculty of Medicine of University of Lisbon)
- FMUC (Faculty of Medicine of University of Coimbra)
- FCML (The Faculty of Medical Sciences of Lisbon)
- FCSUBI (Faculty of Health Sciences of the University of Beira Interior)
- Other (Represent foreigners studying in Portugal at that moment)

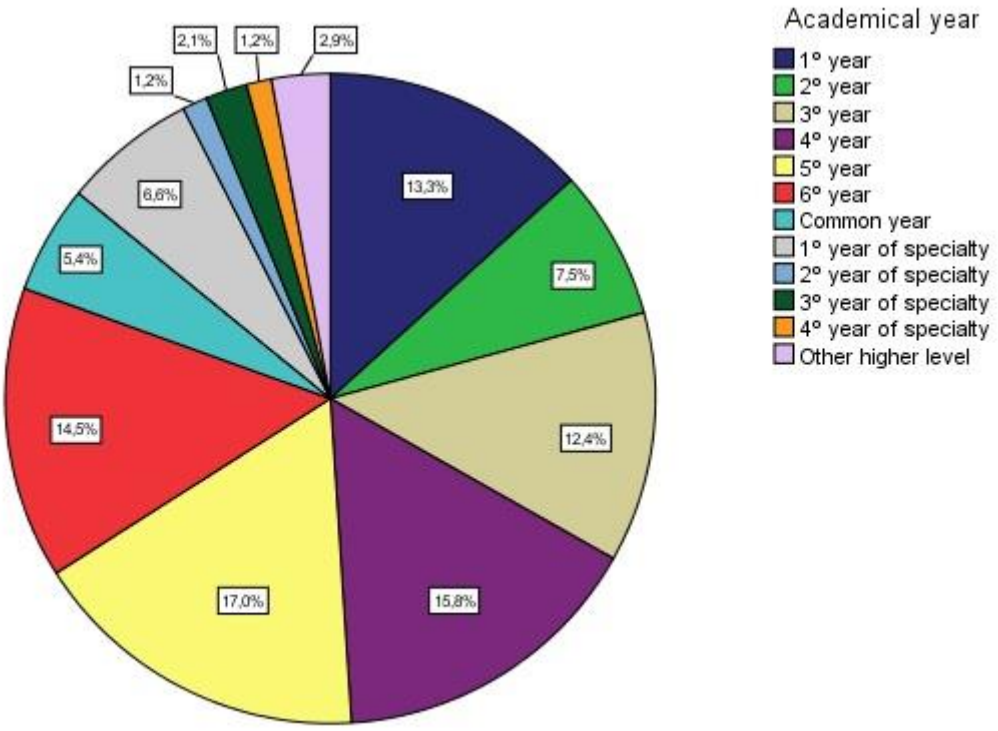

Figure 2 - Distribution of Students by Academical Year

Figure 2 refers to the repartition of the participants by Academical year. Considering this categorization, students who participated more, are part of the first years of the course, which can be classified as students from the integrated Master of Medicine. Therefore, through this chart, it is possible to make the division between 2 large significant groups: integrated Master of Medicine with the total of 80,5% of the answers and 19,5% belonging to students attending the common year, specialty, and other higher levels.

2.2. Data collection

The survey was sent to all the Portuguese Medical Universities by using the email miet1300706@fe.up.pt, addressed directly to the students. In the case of FMUP, it was done through the SIGARRA system, which allows students from the University of Porto to use the dynamic email. The others faculties do not use the same system, consequently the method used was more formal: by telephone and through the institutional email. In addition, it was used the Google Forms platform to insert the questionnaire.

The submission initiated in April 30th, 2015, requesting response via Google forms platform, until the 1st of June. However, by that date, the reply was manifestly insufficient,

so it was required the help from the social networks such as Facebook and Twitter, and also a new email/phone request was sent in 1st of June with a new deadline (the 1st of August, 2015).

Although it would be interesting to have a higher number of answers, further attempts to have extra observations were not fruitful. Therefore, it was necessary to move on with the sample existed until the moment, which consists of 241 students, the majority of which from the north of Portugal. Figure 3 summarizes the process of data collection.

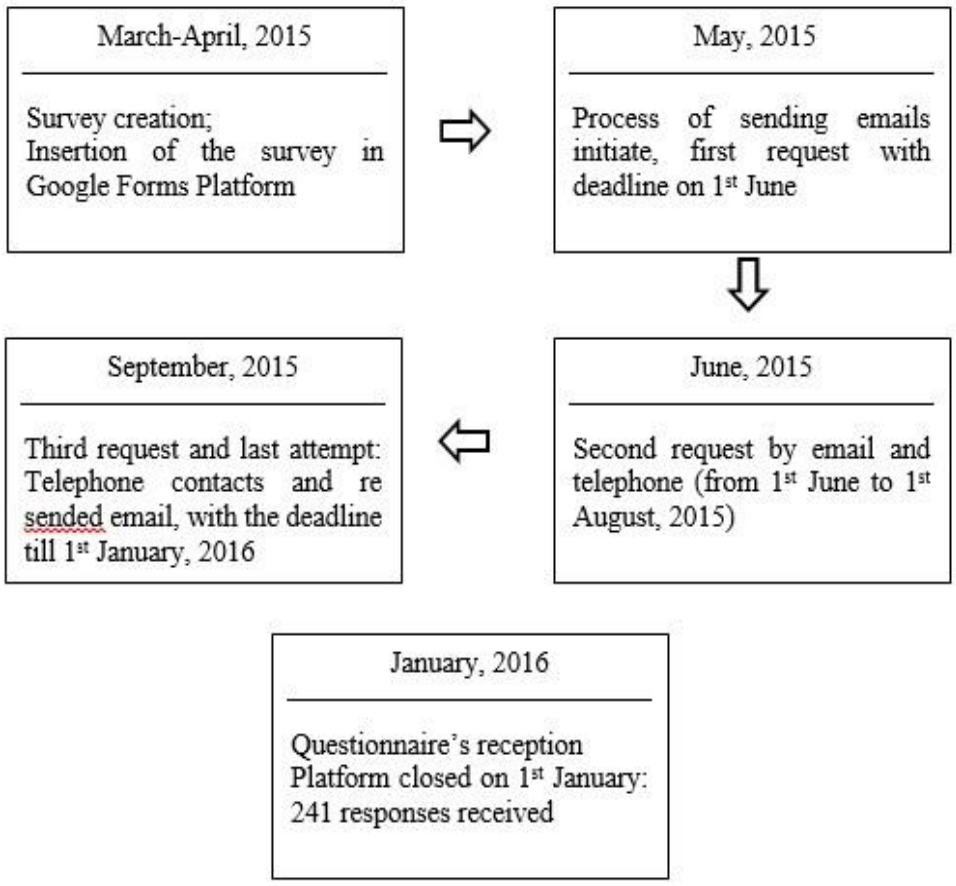

Figure 3 **– The process of Data Collection**

The data was collected by survey and then analyzed statistically by "IBM SPSS Statistics" software.

2.3. Sample

There are 8 Medical University in Portugal according with ANEM (Portuguese Association of Medical Students) 12.000 students are currently enrolled in the Integrated Master of Medicine (2015/2016). Table 2 presents the number of students in the sample by institution.

University	Sample
FMUP	117
FMUL	10
ICBAS	49
FMUC	10
FCML	4
FMUM	10
FCSUBI	2
UA	25
OTHER	15

Table 2 - Sample

3. Results

This chapter presents and describes the statistical analysis of the survey through the SPSS statistics software, which is distributed by 3 main sections: Awareness, Application and Expectation.

As mentioned before, the research tool applied was the survey and it is used to: obtain knowledge of a population, its thoughts and actions; to analyse a social phenomenon through collected data about individuals of the population; in cases where it is essential to study a large number of people (Quivy and Campenhoudt, 2005). As a result this research tool aids this dissertation purposes.

The survey (see Appendices 1 and 2) was developed in Portuguese and in English, considering the target surveyed. It is possible to comprise the survey in 2 parts. The first part addresses the description of the people surveyed: Gender, Age, which university they are attending including the years and medical speciality if appropriate.

The second part addresses the main research questions wherein includes the Awareness, Application and Expectation.

The survey presents: closed-ended questions, which can be categorized as either single questions related to respondents description (where one response is required), dichotomous (where two response items are provided) and multichotomous (where several choices are listed); it also uses a scaled-response questions, in which a scale to measure the attributes is used.

3.1. Awareness

The "Awareness" concerns to the knowledge about this technique from the person surveyed perspective. It includes 3 main questions (see Appendix 1 or 2).

Have you ever heard about 3D Bioprinting?			
	Frequency	**Percent**	**Cumulative Percent**
No	74	30,7	30,7
Yes	167	69,3	100,0
Total	241	100,0	

Table 3 – Frequency table

The first question aims to know whether students are familiar with the concept of 3D Bioprinting. One hundred and sixty seven of the 241 surveyed (69.3%) claim to be knowledgeable of 3D Bioprinting. The remaining 74 surveyed (30.7%) answered that they does not know about technology, as presented in table 3.

In table 4 we present the distribution of answers by gender and in table 5 we conduct a chi-square test to understand the possible correlation between 2 variables, "gender" and the question ("Have you ever heard about 3D Bioprinting")

		Have you ever heard about 3DBioprinting?		Total
		No	**Yes**	
Gender?	**Male**	24	52	76
	Female	50	115	165
Total		74	167	241

Table 4 – Cross tabulation

Test Chi-square					
	Value	df	Level of Sig.	Sig. 2	Sig. 1
Chi-square Pearson	,040	1	,842		
Fisher test				,881	,478
Number of the case	241				

Table 5 - Chi-square test

Considering the results of the Chi-square test, given by a p-value greater than 0, 05, there was not any statistically significant relationship between gender and that question. The highest number of participants surveyed in terms of gender are female with 165 and only 76 for male participants. The level of awareness about 3D Bioprinting as the table refers is positive for both between females and males.

In the second main question, we try to understand how the students came across with 3D Bioprinting.

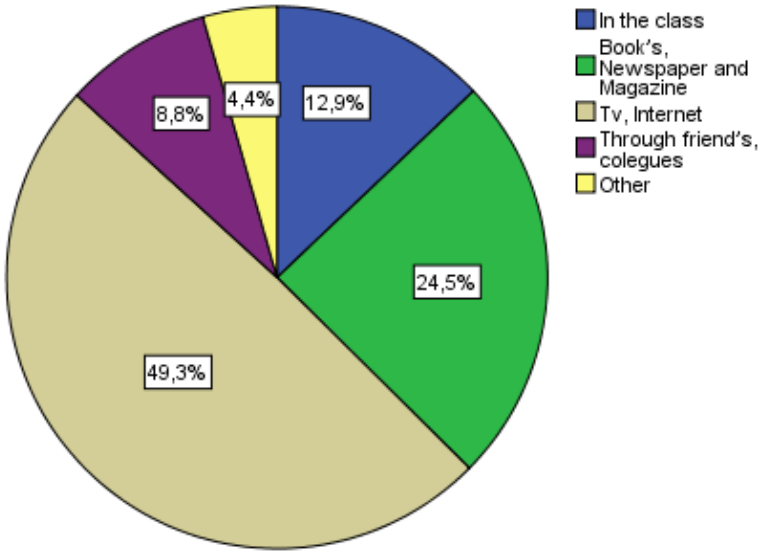

Figure 4 - Circle Graphic

Figure 4 presents the answers to this question. It is clear the most source of knowledge is from Tv and Internet, representing 49,3% of the answers. It was interesting to realise that the information in the class correspond only 12,9%, according to the survey. One of the reasons that could explain this low percentage may be because the subject in question is very uncommon inside the medical Universities in Portugal. The second higher source of knowledge is coming from books, newspaper and magazines, representing 24,5% of the answers.

The last main question in the section of "Awareness" is: -"From your point of view does 3D Bioprinting can be replaced by any other technology? If your answer is yes, please refer which one?"

	Frequency	Percent	Cumulative Percent
No	209	86,7	86,7
Yes	32	13,3	100,0
Total	241	100,0	

Table 6 - Frequency table

Table 6 presents the results. In fact, 86,7% of the respondents does not believe any other existing technology replace 3D Bioprinting, however the last 13,3% of the surveyed mentioned diverse "replacing" technologies, nevertheless many of them can still be used as a complement of 3D Bioprinting technology by itself. Tissue culture and tissues from animal origins was the highest mentioned replacing technologies mentioned by the respondents.

		From your view does 3D Bioprinting can be replaced by any other technology?		
		No. 3D Bioprinting is completely innovative	**Yes**	**Total**
Analysis by age range	**18-20**	44	3	47
	21-23	61	11	72
	24-26	59	11	70
	27-29	26	2	28
	>=30	19	5	24
Total		209	32	241

Table 7 - Cross tabulation

Table 7 details this answer by age and table 8 refers to the analysis between 2 variables: Age range and the question above. The main purpose was to execute a test of chi-square to understand if there was any relationship between these 2 qualitative variables.

Test chi-squad			
	Value	**df**	**Significance level**
Chi-Squad Pearson	4,656	4	,324
Number of cases	241		

Table 8 - Chi-square Test

Considering the results of the Chi-square test the significance level p = value > 0, 05 there was not any statistically significant relationship between age and the question above.

Between 21 till 26 group of ages, we record the highest number of answers and from this point of view there was not any relevant discrepancy reported.

3.2. Application

The Application concerns to where this technology can actually be used. It includes 5 main questions with relevant content. (See Appendix 1 or 2)

Analysis by age range * 3D Bioprinting could be an answer for Transplants? (Q10)

		3D Bioprinting could be an answer for Transplants?						Total
		Nothing Important	Less Important	Little Important	Some Important	Important	Very Important	
Analysis by age range	**18-20**	0	1	4	7	18	17	47
	21-23	3	5	6	22	16	20	72
	24-26	1	6	11	7	27	18	70
	27-29	0	4	1	5	13	5	28
	>=30	0	0	1	12	8	2	23
Total		**4**	**16**	**23**	**53**	**82**	**62**	**240**

Table 9 - Cross tabulation

A question was asked mainly to understand if 3D Bioprinting could be the answer for the Transplants, which by itself it is a huge problem that Humanity has to face, with tendency to increase each year. It was necessary to do a scaled-response questions, in which we use a scale to measure the attributes of the construct, from "Nothing Important" till "Very important". Our goal is to have the opinion of the respondents about the importance of the application of the 3D Bioprinting for organs transplant. The answers are reported in table 9. A vast majority of students consider that 3D Bioprinting is important to solve the problem.

In order to do the Chi-square test it was decided to cross Age and the question above to see if there any statically significant relationship between them.

Test chi-square			
	Value	**Df**	**Significance level**
Chi-square Pearson	41,460	20	,003
Number of cases	241		

Table 10 - Chi-square test

Table 10 presents the results. In fact, the p-value is less than 0,05, suggesting that both groups are different from each other. It can be noticed a statistically significant relationship between age and level of trust about 3D Bioprinting being an answer for transplants. Nevertheless it is important to refer the high number of people that have confidence in the importance related to the application of 3D Bioprinting directed to the transplant of organs. While 34% of the respondents answered "Important", 25, 7 % considered it to be "Very Important". Only 1, 7 % of the people surveyed doesn't believe that 3D Bioprinting could be the solution for the transplants.

Analysis by age range * 3D Bioprinting could be an answer for new drugs investigation? (Q11)

		3D Bioprinting could be an answer for new drugs investigation?						Total
		Nothing important	Less important	Little important	Some important	Important	Very important	
Analysis by age range	**18-20**	0	0	1	13	17	16	47
	21-23	1	2	4	14	26	25	72
	24-26	1	3	3	14	23	26	70
	27-29	0	4	0	2	9	13	28
	>=30	0	1	0	9	11	3	24
Total		2	10	8	52	86	83	241

Table 11 - Cross tabulation

The process was repeated concerning now new drugs investigation. In the Question: 3D Bioprinting could be an answer for new drugs investigation, 34, 4 % of the respondents voted for "Very Important" and 35, 7 % for "Important", less than 1% doesn't believe that could have that purpose. The results are, therefore, very similar to those obtained in the previous question. It is safe to assume that the highest percentage of respondents agreed that 3D Bioprinting can be used not only as a solution for transplants but also to test or create new drugs (i.e., for investigation purposes).

Test chi-square			
	Value	Df	Significance level
Chi-square Pearson	26,009	20	,166
Number of cases	241		

Table 12 - Chi-square test

Table 12 presents the chi-square test for the relationship between age and level of importance reported in the question. As P-value >0, 05, we find there is no statically significant relationship between the variables.

		Please mention in which situation 3DBioprinting could be an asset?					Total
		University environment (Practical classes)	Only for Transplants	Only for new drugs investigation	Transplants and new drugs investigation	None of above	
Analysis by age range	**18-20**	9	4	2	31	1	47
	21-23	14	3	6	45	4	72
	24-26	12	2	5	50	1	70
	27-29	4	2	4	18	0	28
	>=30	6	2	0	16	0	24
Total		45	13	17	160	6	241

Table 13 - Cross tabulation

The state of this technology can be served as a tool for several situations, perhaps the most obvious being:

- University environment perchance practical classes, where the student would be able to use printing organs;
- Like it was mentioned before, a solution for transplants;
- In case of development of drugs and investigation purposes, the printing organs could be definitely an asset (Atala, 2011)

Table 13 refers the number of the respondents that consider each of these situations as more favored to 3D Bioprinting. This question was a multichotomous type of question in which several option items were available. However it is important to underline the fact that some of the options say “Only”: Example: “Only for transplants”; “Only for new drugs, investigation” and the both together. So 18, 7 % of the respondents believe 3D Bioprinting is relevant in Universities in practical class; 5, 4% have confidence it will be

used “Only” for transplants; 7,1% consider that it will be used “Only” for investigation of new drugs; on the other hand, 66,4% of the respondents consider it will be used not only in cases of transplants but it is as well a valuable asset to investigation and testing new drugs.

We executed the chi-square test between age of the respondents and the question: “Please mention in which situation 3D Bioprinting could be an asset”. The P-value is equal to 0,701 > 0, 05, meaning there is no statistically significant relationship between the variables. It was also tested the chi-square test using the variable gender, for which the p-value is equal to 0,412 > 0, 05.

The next question (Question 14 - see Appendices 1 and 2) asks respondents to mention possible constrains about 3D Bioprinting. “Human being mentality” in some cases could be considered a constraint around this technology explicitly in terms of culture habits. Not everyone think the same, which means the technological advance sometimes doesn’t inspire trust to certain individuals. Other option included was “Need”. This option means the need to find a fast solution to a problem; “bureaucratic processes” were also considered as some countries have high bureaucracy systems, which could easily become enormous problem for this technology to enter in the market. “Ethics issues” is another possibility, mainly by doctors, so it was very important to analyze this variable to understand if this is a problem or not for medical students. “Religion” is another option as it not always agrees with science and definitely this technology might create some controversies. Finally, we consider “Economy” as it certainly will take a very important role, since it is important to make investments or no technological advance is ever possible.

The answers to this question reveal that:

- 65, 1% of the respondents does not believe “Human being mentality” can be a constrain for 3D Bioprinting;
- 83, 8% of the respondents does not agree that “Need” is a constrain to 3D Bioprinting;
- 57, 3% of the respondents does not agree that “Bureaucratic processes” is a constrain to 3D Bioprinting;
- 70, 5% of the respondents agree that “Ethics issues” can be a constrain to 3D Bioprinting;

- 75, 5 % of the respondents does not agree that “Religion” is a constrain to 3D Bioprinting;
- 77, 6 % of the respondents does not agree that “Politics” is a constrain to 3D Bioprinting;
- 63, 5% of the respondents agree that “Economy” can be a constrain to 3D Bioprinting;

Question 17: “Do you agree with 3D Bioprinting in mass production?”

	Frequency	Percent	Cumulative Percent
No	107	44,4	44,4
Yes	134	55,6	100,0
Total	241	100,0	

Table 14 – Frequency table

The next question considers the students’ agreement to 3D Bioprinting in mass production, as reported in table 14. Why mass production? This is a consideration about the application of the 3D Bioprinting. As we know the cost of a single unit (unit price principle) can be higher than the aggregation of the product (industry fabrication principle). Of course many of the respondents share the same believe around this subject, which is the risk of banalization of the 3D Bioprinting process. Also some of them mention about the timing, considering that it is not a good idea in the first phase (when entering in the Market), but when the process becomes more mature it may be viable. Furthermore the risk might be too high in comparison with the benefit. Others referred that mass production could be beneficial only for Medical University practical classes.

3.3. Expectation

This section contains the prediction about the technology 3D Bioprinting. The questions formulated to the students are based on the existing literature. Although it may be necessary to do further analyses and take the opinion of the medical community, not only in Portugal but also in other countries, the opinions shared by medical students can provide some insight regarding the future of 3D Bioprinting.

Question 13: “What is your prediction for the 3D Bioprinting technology to be used?”

	Frequency	Percent	Cumulative Percent
5-10 years	83	34,4	34,4
20-40 years	135	56,0	90,5
Next century	18	7,5	97,9
Never	5	2,1	100,0
Total	241	100,0	

Table 15 – Frequency table

The first question (question 13) asks students to predict when 3D Bioprinting will be used, as reported in table 15. The results show that 56% of the respondents have confident that in the next 20-40 years it will be used; however, 34, 4 % believe that 3D Bioprinting will be in the next 5-10 years. Only 7, 5 % of the respondents believe it will be used only in next century and merely 2, 1 % stated that will never be used.

Question 15: As a future Doctor, do you agree with the use of 3D Bioprinting?

	Frequency	Percent	Cumulative Percent
No	8	3,3	3,3
Yes	233	96,7	100,0
Total	241	100,0	

Table 16 - Frequency table

Table 16 considers an interesting question, which is whether, as a future doctor, the respondent agrees with the usage of 3D Bioprinting. It is definitely clear the confidence, from the Medical point of view, regarding the usage of 3D Bioprinting: 96, 7% of the respondents answer favorably to the usage of this technology.

Question 19: Do you agree with this quote “3D Bioprinting is the future of modern medicine”?

	Frequency	Percent	Cumulative Percent
No	96	39,8	39,8
Yes	145	60,2	100,0
Total	241	100,0	

Table 17 - Frequency table

Finally, students are required to answer whether they think that 3D Bioprinting is the future of medicine or not. Table 17 presents the results. According to 60, 2% of the

respondents, it is possible that 3D Bioprinting will be very relevant in the area in the future.

4. Conclusion

This chapter describes an overview of the foremost outcomes of this dissertation, answering the research question based in the information provided. On the other hand it addresses the contributions of this research and refers opportunities for future research.

4.1. Final overview and opportunities for future research

"The world changes materially. Science makes advances in technology and understanding. But the world of humanity doesn't change" (Pierre Schaeffer). The literature review tried to describe the current scenario of 3D Bioprinting. Although some people may look at it with the feeling of a "utopia" situation, slowly this "utopia" can be revealed to be true in the following years. Many real cases already have showed the high potentials to become a real technology of the daily-life for each and every human being.

This dissertation aims to share knowledge about something that may seem unrealistic at the present time, but may be a reality in the future. It was all about the passion behind the possibility to actually save millions and millions of persons. In fact, the application of this technology to organs transplant may not happen in the present but in the future it may be the solution. Nevertheless this dissertation tries to evaluate the impact and acceptance of this technology by the Portuguese Medical Community, by considering the opinions of medicine students.

It is very clear from the subject by itself that the probability of it being the solution for several problems appointed during in the previous chapters is large, but it could also be a disruptive type of Innovation with a breakthrough in the medical field. It can employ many people all over the world, and certainly creating a specific new Market.

"Changing the Shape of Medical Research and Practice, Structurally and functionally accurate bioprinted human tissue models" that's the idea behind Organovo, a company created exclusively with the purpose of design and create functional human tissues by using three-dimensional bioprinting technology. Their goal is definitely build living human tissues that can function exactly like the native tissues each person has. As for the

business model, it is easy to understand the value proposition, they already have several partnerships with biopharmaceutical, academicals medical centers, even now allowing researchers to have the opportunity to test drugs on the functional human tissues.

Without any doubt Organovo is currently doing a great job in order to make the "utopia" becoming something real. This American company is not the only company doing such astonishing work, there are already a few companies, namely in Europe, trying to accomplish the dream.

In conclusion, there are 2 main Research questions in this dissertation:

- The first one is related with the use of the 3DBioprinting in what terms and for what;
- The second is related with the level of acceptance from the medical perception.

These questions are addressed in the methodological and Statistical analysis chapters, giving and overview of the Portuguese situation regarding the awareness and acceptance of this technology. As limitations, the total number of students that actually participated is relatively low and, therefore, this study has to be complemented with further analysis in order to clarify in larger detail the results that were obtained. Naturally, it would be interesting to do a survey such as the one presented here not only in Portugal, but also in other countries, allowing for comparisons.

So as future research, it would be very interesting to develop a deeper study, using newly data, to make comparisons along time and confirm the results. As we know, the technical evolution does not stop, it is always evolving each day, and what is nowadays a "utopia" can be a reality in the future. The results of this study make us very optimistic in terms of the huge chances that 3D Bioprinting has to be a reality applied to the medical world in the future.

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Appendices

Appendice 1 Portuguese Survey

Google Forms

Emerging technology as new-life style. 3D Bioprinting a new era for innovation process

Este inquérito é direccionado apenas para estudantes de Medicina.

Sou vosso colega da Faculdade de Engenharia da Universidade do Porto, estou neste momento elaborar tese de Mestrado relacionado com a tecnologia 3D Bioprinting, que poderá ser considerada uma invenção do sec: XXI não apenas na Medicina moderna mas como também no "State of Art" do processo de Inovação.

Hoje em dia aliando a base da saúde com a capacidade tecnológica é possível a impressão 3D de tecido humano e por sua vez a reprodução através de células retiradas dos pacientes.

O tema vai incidir na reprodução em massa de Orgãos humanos, critérios, previsões, duvidas, tudo isso será base de análise em questão.

Sendo assim a sua ajuda é essencial, apenas 5 minutos podem fazer a diferença.

*Obrigatório

1. Género *
   Marcar apenas uma oval.
   - ◯ Masculino
   - ◯ Feminino

2. Idade? *
   .....

3. Indique a sua instituição de Ensino Superior *
   Marcar apenas uma oval.
   - ◯ Faculdade de Medicina da Universidade do Porto *Após a última pergunta desta secção, passe para a pergunta 8.*
   - ◯ Faculdade de Medicina da Universidade de Lisboa *Após a última pergunta desta secção, passe para a pergunta 8.*
   - ◯ Faculdade de Medicina da Universidade de Coimbra *Após a última pergunta desta secção, passe para a pergunta 8.*
   - ◯ Instituto de Ciências Biomédicas Abel Salazar *Após a última pergunta desta secção, passe para a pergunta 8.*
   - ◯ Faculdade de Ciências Médicas da Universidade Nova de Lisboa *Após a última pergunta desta secção, passe para a pergunta 8.*
   - ◯ Faculdade de Medicina da Universidade do Minho *Após a última pergunta desta secção, passe para a pergunta 8.*
   - ◯ Faculdade de Ciências da Saúde da Universidade da Beira Interior *Após a última pergunta desta secção, passe para a pergunta 8.*
   - ◯ Universidade do Algarve *Após a última pergunta desta secção, passe para a pergunta 8.*
   - ◯ Outra *Após a última pergunta desta secção, passe para a pergunta 7.*

4. Em que fase de formação se encontra? *
Marcar apenas uma oval.

- ◯ 1º ano *Após a última pergunta desta secção, passe para a pergunta 8.*
- ◯ 2º ano *Após a última pergunta desta secção, passe para a pergunta 8.*
- ◯ 3º ano *Após a última pergunta desta secção, passe para a pergunta 8.*
- ◯ 4º ano *Após a última pergunta desta secção, passe para a pergunta 8.*
- ◯ 5º ano *Após a última pergunta desta secção, passe para a pergunta 8.*
- ◯ 6º ano *Após a última pergunta desta secção, passe para a pergunta 8.*
- ◯ Ano comum *Após a última pergunta desta secção, passe para a pergunta 8.*
- ◯ 1º ano / Especialidade *Após a última pergunta desta secção, passe para a pergunta 8.*
- ◯ 2º ano / Especialidade *Após a última pergunta desta secção, passe para a pergunta 8.*
- ◯ 3º ano / Especialidade *Após a última pergunta desta secção, passe para a pergunta 8.*
- ◯ 4º ano / Especialidade *Após a última pergunta desta secção, passe para a pergunta 8.*
- ◯ Outra *Após a última pergunta desta secção, passe para a pergunta 6.*

5. Especialidade (Se ainda não sabe, responda "Não sei") *
Por favor indique qual:

.....

Master in Innovation and Technological Entrepreneurship
(FEUP-FEP)

6. Indique outra fase de formação *

Master in Innovation and Technological Entrepreneurship
(FEUP-FEP)

7. Indique outra instituição de ensino *

Master in Innovation and Technological Entrepreneurship
(FEUP-FEP)

8. Já ouviu falar sobre a Tecnologia 3D Bioprinting? *
Marcar apenas uma oval.

- ◯ Sim *Passe para a pergunta 9.*
- ◯ Não *Passe para a pergunta 10.*

9. Em que âmbito? *
   Marcar tudo o que for aplicável.

   - [ ] Nas aulas
   - [ ] Livros, Jornais, Revistas
   - [ ] Televisão, Internet
   - [ ] Através de amigos,colegas
   - [ ] Outra

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(FEUP-FEP)

10. Até que ponto a impressão de orgão humanos poderá ser a resposta para Transplantes *
    Indique a sua importância mediante a escala
    Marcar apenas uma oval.

0	1	2	3	4	5
◯	◯	◯	◯	◯	◯

11. Até que ponto a impressão de orgão humanos poderá ser a resposta para testar novos Medicamentos (Investigação) *
    Indique a sua importância mediante a escala
    Marcar apenas uma oval.

0	1	2	3	4	5
◯	◯	◯	◯	◯	◯

12. Mediante as respostas anteriores. Refira em que situação a impressão de orgãos poderá ser uma mais valia: *
    Tenha atenção na resposta
    Marcar apenas uma oval.

    - ◯ Ambiente universitário (aulas praticas)
    - ◯ Apenas em relação aos Transplantes
    - ◯ Apenas no tratamento de novos Medicamentos (Investigação)
    - ◯ Transplantes e testar novos medicamentos
    - ◯ Nenhuma das anteriores

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(FEUP-FEP)

13. Qual a sua previsão para que Tecnologia 3D Bioprinting seja efectivamente usada *
Marcar apenas uma oval.

- ◯ 5-10 anos
- ◯ 20-40 anos
- ◯ No próximo século
- ◯ Nunca

14. As limitações desta tecnologia estão directamente ligadas *
Marcar tudo o que for aplicável.

- ☐ Mentalidade do ser humano
- ☐ Necessidade
- ☐ Processos burocráticos
- ☐ Questão de etica
- ☐ Religião
- ☐ Politica
- ☐ Economia
- ☐ Nenhuma das anteriores

15. Como futuro Médico concorda com a utilização da impressão 3D de tecido humano *
Do ponto de vista da sua aceitação
Marcar apenas uma oval.

- ◯ Sim *Passe para a pergunta 17.*
- ◯ Não *Passe para a pergunta 16.*

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16. Indique a razão de não concordar com a impressão 3D de tecido humano *

.....

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17. Concorda com a impressão 3D em massa *
Do ponto de vista da sua utilização
Marcar apenas uma oval.

- ◯ Sim *Passe para a pergunta 19.*
- ◯ Não *Passe para a pergunta 18.*

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18. Indique a razão de não concordar com a impressão 3D em massa *

.....

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19. Concorda com a seguinte afirmação " 3D Bioprinting é o futuro da Medicina moderna" *
Marcar apenas uma oval.

- ◯ Sim *Após a última pergunta desta secção, passe para a pergunta 21.*
- ◯ Não *Após a última pergunta desta secção, passe para a pergunta 21.*

20. Na sua perspectiva a utilização desta tecnologia poderá ser substituta de outra tecnologia já utilizada *
Marcar apenas uma oval.

- ◯ Sim
- ◯ Não. 3D Bioprinting é totalmente inovadora *Pare de preencher este formulário.*

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21. Indique qual é a tecnologia: *

.....

Appendice 2 English Survey

Emerging technology as new-life style. 3D Bioprinting a new era for innovation process

This survey is restricted only for medical students.

I´m a student at the Faculty of Engineering of University of Porto. I am currently doing a Master thesis related with 3D Bioprinting technology, which can be considered an invention of sec: XXI not only in modern medicine but as well as in the “State of Art” of innovation process.

Nowadays combining the basis of health with the high technological capability it is possible to print human tissue, using as ink human cells.

The subject will focus on the mass reproduction of human organs, criteria, predictions, questions, all this will be analysis base in question.

Therefore your help is essential, only 5 minutes can make the difference.

*Mandatory

1.Gender ?*

Mark only one oval.

- ◯ Masculino
- ◯ Feminino

2.Age? *

.....

3.Which University are you attending? *

Mark only one oval..

- ◯ Faculty of Medicine of University of Porto *After the last question in this section, go to question 8*
- ◯ Faculty of Medicine Of University of Lisbon *After the last question in this section, go to question 8*
- ◯ Faculty of Medicine of University of Coimbra *After the last question in this section, go to question 8*
- ◯ Institute of Biomedical Sciences Abel Salazar of U.Porto *After the last question in this section, go to question 8*
- ◯ Faculty of Medical Sciences of Lisbon *After the last question in this section, go to question 8*
- ◯ Faculty of Medicine of University of Minho *After the last question in this section, go to question 8*
- ◯ Faculty of Health Sciences of the University of Beira Interior *After the last question in this section, go to question 8*
- ◯ Algarve University *After the last question in this section, go to question 8*
- ◯ Other *After the last question in this section, go to question 7*

4.In what academical phase are you in? *

Make only one oval.

- 1º year *After the last question in this section, go to question 8.*
- 2º year *After the last question in this section, go to question 8.*
- 3º year *After the last question in this section, go to question 8.*
- 4º year *After the last question in this section, go to question 8.*
- 5º year *After the last question in this section, go to question 8.*
- 6º year *After the last question in this section, go to question 8.*
- Common year *After the last question in this section, go to question 8.*
- 1º year / Specialty *After the last question in this section, go to question 8.*
- 2º year / Specialty *After the last question in this section, go to question 8.*
- 3º year / Specialty *After the last question in this section, go to question 8*
- 4º year / Specialty *After the last question in this section, go to question 8.*
- Other higher level *After the last question in this section, go to question 6.*

5.Specialty (If you don´t know the answer please say " I do not know")

Please specify which one:

.....

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6. Can you mention another academical phase, please? *

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7. Please refer other University? *

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8. Have you ever heard about 3D Bioprinting? *

Mark only one oval.

- Yes *Go to question 9.*
- No *Go to question 10.*

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9.In which context? *

More than one option can be choose.

- [ ] At the class
- [ ] Books, newspaper, magazine
- [ ] Television, Internet
- [ ] Through friends, colegues
- [ ] Other

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10. 3D Bioprinting could be an answer for Transplants? *

Refer the level of importance by using the scale

Mark only one oval.

	0	1	2	3	4	5
	◯	◯	◯	◯	◯	◯

11.3D Bioprinting could be an answer for new drugs investigation*

Refer the level of importance by using the scale

Mark only one oval.

	0	1	2	3	4	5
	◯	◯	◯	◯	◯	◯

12. According to the previous answer, please mention in which situation 3D Bioprinting could be an asset: *

Beware in which answer you will choose

Mark only one oval.

- ◯ University environment (Practical classes)
- ◯ Only for transplants
- ◯ Only for new drugs (Investigation)
- ◯ Transplants and new drugs investigation
- ◯ None of above

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13.What is your prediction for the 3D Bioprinting technology can be used? *

Mark only one oval.

- ◯ 5-10 years
- ◯ 20-40 years
- ◯ Next century
- ◯ Never

14.Possible constrains of 3D Bioprinting could be through *

Mark more than one if you want.

- ☐ Human mentality
- ☐ Need
- ☐ Bureaucratic processes
- ☐ Ethics issues
- ☐ Religion
- ☐ Politics
- ☐ Economy
- ☐ None of above

15.As a future Doctor, do you agreed with the use of 3D Bioprinting? *

From the point of view of its acceptance

Mark only one oval.

- ◯ Yes *Go to queston 17.*
- ◯ No *Go to question 16.*

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16.If you don´t agreed, please refer why? *

.....

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17.Do you agreed with 3D Bioprinting in mass production *

From the point of view of its use

Mark only one oval.

- ◯ Yes *Go to question 19.*
- ◯ No *Go to question 18.*

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18.If you don´t agreed, please refer why? *

.....

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19.Do you agree with this quote " 3D Bioprinting is the future of modern medicine" *
Mark only one oval.

- ◯ Yes *After the last question in this section, go to question 21.*
- ◯ No *After the last question in this section, go to question 21.*

20.From your view does 3D Bioprinting can be replaced by any other techonology *
Mark only one oval.

- ◯ Yes
- ◯ No. 3D Bioprinting is completely innovative

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21. Which technology can replace 3D Bioprinting: *

.....

Appendice 3 Frequency Statitics

		Frequency statistics																	
		Total (N=241; 100%)		FMUP (N=117; 48,5%)		FMUL (N=10; 4,1%)		FMUC (N=9; 3,7%)		ICBAS (N=49; 20,3%)		FCMUNL (N=4; 1,7%)		FMUM (N=10; 4,1%)		FCSUBI (N=2; 0,8%)		UA (N=25; 10,4%)		Other (N=15; 6,2%)	
Variable	Answer	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Gender	Male	76	31,5	37	31,6	2	20,0	3	33,3	10	20,4	1	25,0	3	30,0	2	100,0	11	44,0	7	46,7
	Female	165	68,5	80	68,4	8	80,0	6	66,7	39	79,6	3	75,0	7	70,0			14	56,0	8	53,3
Academical year	1° year	32	13,3	16	13,7	2	20,0			8	16,3	1	25,0					2	8,0	3	20,0
	2° year	18	7,5	14	12,0			1	11,1	1	2,0									2	13,3
	3° year	30	12,4	13	11,1	2	20,0	2	22,2	6	12,2			2	20,0			5	20,0		
	4° year	38	15,8	13	11,1			2	22,2	14	28,6	1	25,0		0			6	24,0	2	13,3
	5° year	41	17,0	28	23,9	2	20,0			6	12,2			1	10,0	1	50,0	3	12,0		
	6° year	35	14,5	17	14,5	1	10,0			5	10,2	1	25,0	2	20,0			8	32,0	1	6,7
	Common year	13	5,4	3	2,6	1	10,0	2	22,2	6	12,2									1	6,7
	1° year of specialty	16	6,6	8	6,8	2	20,0			1	2,0	1	25,0	3	30,0	1	50,0				
	2° year of specialty	3	1,2	4	3,4			1	11,1											2	13,3
	3° year of specialty	5	2,1	1	,9													1	4,0		
	4° year of specialty	3	1,2	16	13,7					1	2,0			1	1,0						
	Other higher level	7	2,9					1	11,1	1	2,0			1	1,0					4	26,7
Have you ever heard about 3DBioprinting	Affirmative answer	167	69,3	82	70,1	2	20,0	6	66,7	41	83,7	1	25,0	10	100,0	1	50,0	16	64,0	7	46,7
Where did you heard about 3D Bioprinting	In class	38	15,8	14	12,0	1	10,0	1	11,1	11	22,4			7	70,0	1	50,0	1	4,0	2	13,3
	Book's, Newspaper and Magazine	72	29,9	33	28,2	2	20,0	2	22,2	13	26,5	1	25,0	7	70,0	1	50,0	8	32,0	5	33,3
	Tv, Internet	145	60,2	71	60,7	2	20,0	6	66,7	39	79,6	1	25,0	9	90,0			11	44,0	6	40,0
	Friend's, colegues	26	10,8	11	9,4			1	11,1	4	8,2	1	25,0	4	40,0			3	12,0	2	13,3
	Other	13	5,4	5	4,3					6	12,2	1	25,0	1	10,0						
3DBioprinting could be an asset for:	University environment (Practical classes)	45	18,7	29	24,8	3	30,0	1	11,1	7	14,3			1	10,0			4	16,0		
	Only for Transplants	13	5,4	6	5,1	1	10,0			3	6,1							2	8,0	1	6,7
	Only for new drugs investigation	17	7,1	5	4,3	2	20,0	1	11,1			0	0	2	20,0			3	12,0	4	26,7
	Transplants and new drugs investigation	160	66,4	74	63,2	4	40,0	7	77,8	38	77,6	3	75,0	7	70,0	2	100,0	15	60,0	10	66,7

	None of above	6	2,5	3	2,6					1	2,0	1	25,0					1	4,0		
Prediction for 3DBioprinting	5-10 years	83	34,4	41	35,0	4	40,0	3	33,3	5	10,2			9	90,0	1	50,0	15	60,0	5	33,3
	20-40 years	135	56,0	63	53,8	5	50,0	5	55,6	39	79,6	3	75,0	1	10,0			10	40,0	9	60,0
	Next century	18	7,5	12	10,3	1	10,0			3	6,1	1	25,0							1	6,7
	Never	5	2,1	1	0,9			1	11,1	2	4,1					1	50,0				
Possible constrains of 3DBioprinting:	Human being mentality	84	34,9	43	36,8	5	50,0	2	22,2	16	32,7			3	30,0	1	50,0	7	28,0	7	46,7
	Need	39	16,2	21	17,9	4	40,0	1	11,1	8	16,3							1	4,0	4	26,7
	Bureaucratic processes	103	42,7	48	41,0	6	60,0	1	11,1	25	51,0	1	25,0	5	50,0	2	100,0	11	44,0	4	26,7
	Ethics issues	170	70,5	83	70,9	8	80,0	6	66,7	38	77,6	4	100,0	8	80,0	2	100,0	14	56,0	7	46,7
	Religion	59	24,5	30	25,6	5	50,0	3	33,3	11	22,4	1	25,0	2	20,0	2	100,0	3	12,0	2	13,3
	Politics	54	22,4	26	22,2	2	20,0			13	26,5	1	25,0	5	50,0	1	50,0	4	16,0	2	13,3
	Economy	153	63,5	74	63,2	8	80,0	6	66,7	32	65,3	3	75,0	6	60,0	2	100,0	13	52,0	9	60,0
	None of above	18	7,5	9	7,7					3	6,1							5	20,0	1	6,7
Do you agree with 3DBioprinting(Medical Point of view)	Yes	233	96,7	114	97,4	10	100,0	9	100,0	48	98,0	4	100,0	10	100	2	100,0	24	96,0	12	80,0
If you dont agreed, why:	Ethics	4	1,7			4	40,0			1	2,0							1	4,0	2	13,3
	n.a.	4	1,7	3	2,6	2	20,0													1	6,7
Do you agreed with 3DBioprinting in mass production	Yes	134	55,6	65	55,6	3	30,0	5	55,6	21	42,9	3	75,0	6	60,0	2	100,0	18	72,0	11	73,3
If you dont agreed, why:	Only as last resource	1	,4	1	,9																
	Only for different reason	1	,4	1	,9																
	Only for practical class's	1	,4															1	4,0		
	After process maturity	2	,8	2	1,7																
	Trivialization of the process	34	14,1	13	11,1			3	55,6	11	22,4	1	25,0	2	20,0			4	16,0		
	Control/Legislation	6	2,5	2	1,7					2	4,1			1	10,0					1	6,7
	Social differentiation	1	,4	1	,9																
	Economy	2	,8	2	1,7																
	Ethics	23	9,5	11	9,4	4	40,0			6	12,2			1	10,0					1	6,7
	n.a.	10	4,1	5	4,3	2	20,0			2	4,1									1	6,7
	Prudence between risk taken and benefit's	2	,8	1	,9					1	2,0										

	Custom process	21	8,7	11	9,4	1	10,0	1	11,1	6	12,2							1	4,0	1	6,7
	Fear negative consequences	1	,4	1	,9																
	No relevance	1	,4	1	,9																
	Illegal organ trade	1	,4															1	4,0		
Do you agree with this quote "3DBioprinting is the future of modern medicine"	Yes	145	60,2	69	59,0	5	50,0	7	77,8	26	53,1	3	75,0	10	100,0	1	50,0	12	48,0	12	80,0
3D Bioprinting can be replaced by any other technology?	**No. 3D Bioprinting is completely innovative**	**209**	**86,7**	**95**	**81,2**	9	90,0	8	88,9	46	93,9	4	100,0	10	100,0	2	100,0	24	96,0	11	73,3
	Alo-enxerts and alo-transplants	2	,8	2	1,7																
	Tissue culture	9	3,7	7	6,0					1	2,0							1	4,0		
	Complementary diagnostic exams	1	,4	1	,9																
	n.a.	11	4,6	7	6,0					1	2,0									3	20,0
	Pacemaker	1	,4	1	,9																
	Prostheses	1	,4	1	,9																
	Tissues from Technical Bio-products	2	,8	2	1,7					1	2,0										
	Tissues from animal origin	1	,4	1	,9																
	Replacement techniques of organ function	1	,4	2	1,7	1	10,0														
	Technology	1	,4																	1	6,7
	Organ trade	1	,4	1	,9																